

October 30, 2013

LCDR Christopher Steele
Office of Naval Research
Code 34 – Warfighter Performance
875 N. Randolph St.
Arlington, VA 22203-1995

Subject: Quarterly Performance/Technical Report of the National Marrow Donor Program®

Reference: Grant Award #N00014-12-1-0142 between the Office of Naval Research and the National Marrow Donor Program

Dear LCDR. Steele:

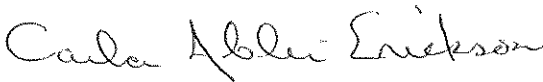
Enclosed is subject document which provides the performance activity for each statement of work task item of the above reference for the period of July 1, 2013 to September 30, 2013.

Should you have any questions as to the scientific content of the tasks and the performance activity of this progress report, you may contact our Chief Medical Officer – Dennis L Confer, MD directly at 612-362-3425.

With this submittal of the quarterly progress report, the National Marrow Donor Program has satisfied the reporting requirements of the above reference for quarterly documentation. Other such quarterly documentation has been previously submitted under separate cover.

Please direct any questions pertaining to the cooperative agreement to my attention at 612-362-3403 or at cabler@nmdp.org.

Sincerely,



Carla Abler-Erickson, MA
Contracts Manager

Enclosure: Quarterly Report with SF298

C: J. Kabisch – ACO (ONR-Chicago)
Dr. Robert J. Hartzman, CAPT, MC, USN (Ret)
Jennifer Ng, PhD – C.W. Bill Young Marrow Donor Recruitment and Research Program
J. Rike - DTIC (Ste 0944)
NRL (Code 5227)
Dennis Confer, MD, Chief Medical Officer, NMDP
Stephen Spellman

REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
<small>Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Service, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188) Washington, DC 20503.</small>					
PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE (DD-MM-YYYY) 30-10-2013		2. REPORT TYPE Quarterly		3. DATES COVERED (From - To) Jul 2013 – Sep 2013	
4. TITLE AND SUBTITLE Development of Medical Technology for Contingency Response to Marrow Toxic Agents - Quarterly Performance/Technical Report for July 01, 2013 to September 30, 2013 Period 7				5a. CONTRACT NUMBER N/A	
				5b. GRANT NUMBER N00014-12-1-0142	
				5c. PROGRAM ELEMENT NUMBER N/A	
6. AUTHOR(S) Spellman, Stephen				5d. PROJECT NUMBER N/A	
				5e. TASK NUMBER Project 1, 2, 3, 4	
				5f. WORK UNIT NUMBER N/A	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) National Marrow Donor Program 3001 Broadway St., N.E., Ste. 500 Minneapolis, MN 55413				8. PERFORMING ORGANIZATION REPORT NUMBER N/A	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) Office of Naval Research 875 N. Randolph St. Arlington, VA 22203				10. SPONSOR/MONITOR'S ACRONYM(S) ONR	
				11. SPONSORING/MONITORING AGENCY REPORT NUMBER N/A	
12. DISTRIBUTION AVAILABILITY STATEMENT Approved for public release; distribution is unlimited					
13. SUPPLEMENTARY NOTES N/A					
14. ABSTRACT <u>1. Contingency Preparedness:</u> Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan. <u>2. Rapid Identification of Matched Donors :</u> Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event. <u>3. Immunogenetic Studies:</u> Increase understanding of the immunologic factors important in HSC transplantation. <u>4. Clinical Research in Transplantation:</u> Create a platform that facilitates multicenter collaboration and data management.					
15. SUBJECT TERMS Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes					
16. SECURITY CLASSIFICATION OF:		17. LIMITATION OF ABSTRACT Same as Report		18. NUMBER OF PAGES 19	
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U	19a. NAME OF RESPONSIBLE PERSON Dennis L. Confer, MD – Chief Medical Office		
			19b. TELEPHONE NUMBER (Include area code) 612.362.3425		

Grant Award N00014-12-1-0142

DEVELOPMENT OF MEDICAL TECHNOLOGY
FOR CONTINGENCY RESPONSE TO MARROW TOXIC AGENTS
QUARTERLY
PERFORMANCE / TECHNICAL REPORT
FOR
JULY 01, 2013 to SEPTEMBER 30, 2013
PERIOD 7

Office of Naval Research

And

The National Marrow Donor Program
3001 Broadway Street N.E.
Minneapolis, MN 55413
1-800-526-7809

QUARTER PROGRESS REPORT**Development of Medical Technology for Contingency Response to Marrow Toxic Agents****July 01, 2013 through September 30, 2013**

TABLE OF CONTENTS			
TASK	DESCRIPTION	STATUS	PAGE
IIA	Contingency Preparedness		
IIA.1	Objective 1 – Care Plans by Transplant Physicians		
	Task 1 – Secure Interest of Transplant Physicians	Open	4
	Task 2 – GCSF in Radiation Exposure	No Activity	4
	Task 3 – Patient Assessment Guidelines	No Activity	4
	Task 4 – National Data Collection and Management Model	Closed	4
IIA.2	Objective 2 – Coordination of Care of Casualties		
	Task 1 – Contingency Response Network	Open	4
	Task 2 – Standard Operating Procedures	No Activity	6
IIA.3	Objective 3 – Information Technology Infrastructure		
	Task 1 – Disaster Recovery	Closed	6
	Task 2 – Critical Facility and Staff Related Functions	No Activity	6
II.B	Rapid Identification of Matched Donors		
II.B.1	Objective 1 – Resolution of Speeds Donor Selection		
	Task 1 – Increase Registry Diversity	No Activity	7
	Task 2 – Evaluate HLA-DRB1 High Resolution Typing	Closed	7
	Task 3 – Evaluate HLA-C Typing of Donors	Closed	7
	Task 4 – Evaluate Buccal Swabs	Open	7
	Task 5 – Enhancing HLA Data for Selected Donors	Closed	8
	Task 6 – Maintain a Quality Control Program	Open	8
IIB.2	Objective 2 – Improve HLA Quality & Resolution		
	Task 1 – Collection of Primary Data	No Activity	8
	Task 2 – Validation of Logic of Primary Data	Closed	8
	Task 3 – Reinterpretation of Primary Data	Closed	8
	Task 4 – Genotype Lists & Matching Algorithm	No Activity	8
IIB.3	Objective 3 – Algorithm to Predict Best Donor		
	Task 1 – Incorporate Frequencies into Matching Algorithm	No Activity	9
	Task 2 – Enhancement of EM Algorithm	Open	9
	Task 3 – Optimal Registry Size Analysis	Open	9
	Task 4 – Target Underrepresented Phenotypes	Open	10

QUARTER PROGRESS REPORT**Development of Medical Technology for Contingency Response to Marrow Toxic Agents****July 01, 2013 through September 30, 2013**

	Task 5 – Bioinformatics Web Site	No Activity	10
	Task 6 – Utilize Search Strategy Advisors to Improve Algorithm	No Activity	10
	Task 7 – Population Genetics	Closed	11
	Task 8 – Haplotype Matching	Closed	11
	Task 9 – Global Haplotype/Benchmark	Closed	11
IIB.4	Objective 4 – Reduction of Donor Matching Time		
	Task 1 – Expand Network Communications	Closed	11
	Task 2 – Central Contingency Management	Open	11
	Task 3 – Benchmarking Analysis	Closed	12
	Task 4 – Expand Capabilities of Collection and Apheresis Centers	Closed	12
IIC.	Immunogenetic Studies		
IIC.1	Objective 1 – Influence of HLA Mismatches		
	Task 1 – Donor Recipient Pair Project	Open	12
IIC.2	Objective 2 – Role of Other Loci and GVHD		
	Task 1 – Analysis of Non-HLA Loci	Open	12
	Task 2 – Related Pairs Research Repository	Closed	13
	Task 3 – CIBMTR Integration	Closed	13
IID	Clinical Research in Transplantation		
IID.1	Objective 1 – Clinical Research Improves Outcomes		
	Task 1 – Observational Research, Clinical Trials and NIH Transplant Center	Open	13
	Task 2 – Research with NMDP Donors	Closed	13
	Task 3 – Expand Immunobiology Research	Open	14
	Acronym List		16

QUARTER PROGRESS REPORT**Development of Medical Technology for Contingency Response to Marrow Toxic Agents****July 01, 2013 through September 30, 2013**

IIA. Contingency Preparedness – Objective 1: Recovery of casualties with significant myelosuppression following radiation or chemical exposure is optimal when care plans are designed and implemented by transplant physicians

IIA.1 Task 1: Secure Interest of Transplant Physicians	Period 5 Activity: <ul style="list-style-type: none"> Held the first RITN mobile training version of the Advanced Medical Response to a Radiological Disasters conducted by Radiation Emergency Assistance Center and Training Site staff at Duke University in August, training over 50 medical staff
IIA.1 Task 2: GCSF in Radiation Exposure	Period 7 Activity: <ul style="list-style-type: none"> No activity this period.
IIA.1 Task 3: Patient Assessment Guidelines and System Enhancements	Period 7 Activity: <ul style="list-style-type: none"> No activity this period.

IIA 1 Task 4: National Data Collection Model – This task is closed.

IIA. Contingency Preparedness – Objective 2: Coordination of the care of casualties who will require hematopoietic support will be essential in a contingency situation.

IIA.2 Task 1: Contingency Response Network	Period 5 Activity: <ul style="list-style-type: none"> Held two (2) Web based Tabletop Exercises for RITN centers <ul style="list-style-type: none"> One exercise was for central US hospitals and the other was for western hospitals This afforded 17 hospitals to discuss in an open forum how they would respond to a mass casualty incident to learn from each other's response Held a joint conference with the Centers for Medical Counter Measures against Radiation (NIAID-CMCR) and RITN conference in Baltimore July 31-Aug 2; <ul style="list-style-type: none"> The conference purpose and scope were: <ul style="list-style-type: none"> The tremendous environmental, social, and medical cost of a large-scale release of nuclear or radiological material as a result of deliberate attack or natural disaster has led to several
---	---

QUARTER PROGRESS REPORT**Development of Medical Technology for Contingency Response to Marrow Toxic Agents****July 01, 2013 through September 30, 2013**

	<p>programs aimed at improving national and local preparedness.</p> <ul style="list-style-type: none">▪ The Radiation Injury Treatment Network (RITN) and the Centers for Medical Countermeasures against Radiation (CMCR) convened a three-day workshop on the Mitigation and Treatment of Radiation Damage from July 31st to August 2nd, 2013 that covered patient assessment, biomarkers and biodosimetry, suitability of animal models, small molecules, growth factors, and cells as mitigators, as well as their mechanisms of action in radiation-damaged tissues, late effects of acute and prolonged exposure, survivorship issues, and future developments. The workshop was held at the historic Tremont Plaza Hotel.▪ The meeting provided an open forum for invited and plenary speakers and discussants to assess progress on issues related to radiation injury, mitigation and treatment. Various radiation scenarios were presented along with novel approaches at multiple stages of development. <ul style="list-style-type: none">○ The agenda included:<ul style="list-style-type: none">▪ Keynote Address: Preparedness and Response to Radiation▪ Possible Radiological Incident Scenarios▪ Casualty Triage and Distribution▪ The RITN Response to Radiological Scenarios▪ Emergency Management from the CMCR perspective▪ Workshop 1: Biodosimetry and Biomarkers - assessing the need▪ Animal Models of Radiation Damage and Confounders▪ The Challenge underlying Radiation Mitigation▪ Workshop 2: Small Molecule Radiation Mitigators▪ Workshop 3: Growth Factors and Cytokines as Mitigators▪ Workshop 4: Cell Replacement Approaches for Radiation Mitigation
--	--

QUARTER PROGRESS REPORT**Development of Medical Technology for Contingency Response to Marrow Toxic Agents****July 01, 2013 through September 30, 2013**

	<ul style="list-style-type: none"> ▪ Workshop 5: Mitigation and Treatment of Late Effects ▪ Identification of the Grand Challenges in Radiation Mitigation and Treatment ○ Conference evaluation results: <ul style="list-style-type: none"> ▪ 95 attendees completed the evaluation (of 172 registrants) ▪ 27 physicians requested CME ▪ 53 attendees requested contact hours, nursing credits or med tech credits ▪ Workshop ratings on a scale of 1 to 5 (5 as the highest rating): <ul style="list-style-type: none"> • Overall Rating of the Workshop: 4.55 • The information presented applies to my work: 4.45 • The instructional materials helped me to understand the content: 4.10 • The program was well organized: 4.55 • I learned new knowledge & skills from this session: 4.45
IIA.2 Task 2: Sibling Typing Standard Operating Procedures	Period 7 Activity: <ul style="list-style-type: none"> • No activity this period.
IIA. Contingency Preparedness – Objective 3: NMDP's critical information technology infrastructure must remain operational during contingency situations that directly affect the Coordinating Center.	
IIA.3 Task 1: I.S. Disaster Recovery – This task is closed.	
IIA.3 Task 2: Critical Facility and Staff Related Functions	Period 7 Activity: <ul style="list-style-type: none"> • No activity this period.

QUARTER PROGRESS REPORT

Development of Medical Technology for Contingency Response to Marrow Toxic Agents

July 01, 2013 through September 30, 2013

IIB. Rapid Identification of Matched Donors – Objective 1: Increasing the resolution and quality of the HLA testing of volunteers on the registry will speed donor selection.

IIB.1 Task 1:
Increase Registry
Diversity

Period 7 Activity:

- No activity this period.

IIB.1 Task 2: Evaluate HLA-DRB1 High Res typing – This task is closed.

IIB.1 Task 3: Evaluate HLA-C Typing of Donors – This task is closed

IIB.1 Task 4:
Evaluate Buccal
Swabs

Period 7 Activity:

- Frozen Buccal Swab Feasibility Study:
 - Previously stored buccal swab samples were identified for 10 donors; one of the two remaining swabs was temporarily stored frozen at -30°C for one week (just the swab tip in a screw-cap vial). Both swabs (room temperature and frozen) for each donor were sent to the typing laboratory for evaluation of quality of DNA, quantity of DNA, and high resolution HLA characterization. Results indicate there were no differences in the laboratory's ability to correctly HLA type the temporarily frozen samples. There was also no observed degradation of the DNA quality or quantity when buccal swab samples were frozen. The lab did comment on the difficulty of using just the swab tips and their concern with contamination when handling samples.
 - Study above was repeated with an additional 10 donors, freezing the intact full length swab in a plastic bag. Laboratory repeated testing and again found no differences in HLA typing or DNA quantity and quality with using plastic bags for storage of the frozen samples. Lab also commented that the handling of samples in the plastic bags is similar to the current processes and no concerns with contamination using this approach.
 - A larger study will evaluate a cohort of QC donors. The study will compare swabs stored at room temperature, -30°C, and -80°C for quality of DNA, quantity of DNA, and high resolution HLA characterization. An NMDP IRB application for Bio-Medical Studies was submitted and approved and the study will begin enrolling volunteer QC donors and collecting samples next quarter.

QUARTER PROGRESS REPORT**Development of Medical Technology for Contingency Response to Marrow Toxic Agents****July 01, 2013 through September 30, 2013****IIB 1 Task 5:** Enhancing HLA Data for Selected Donors – This task is closed.**IIB 1 Task 6:**

Maintain a Quality Control Program

Period 7 Activity:

During this quarter, 19 additional cell lines were received from the cell processing laboratory and incorporated into the regular QC rotation, bringing the total number of B-LCL QC Master lots obtained from this grant to 59. Of the 133 cells lines selected for incorporation into the QC program in FY2012, 74 exhibited negative cell growth (44% cell culture success rate). As of September 30, 2013, 534 QC Masters were in active rotation. The highest volume recruitment laboratory is challenged with a unique QC Master every 7.5 weeks, 5.2 weeks at peak volume.

Work continued on the pilot study to assess the feasibility of using purified DNA as an alternative QC sample type, in order to decrease the cost of the QC program. The laboratory that experienced issues with the purified DNA swabs in phase II tested another set of samples. The laboratory was able to successfully type all 8 samples. Two additional DNA extraction laboratories were identified, and five ml of frozen blood aliquots from 5 unique volunteer QC donors were shipped. Assessment of DNA yield is underway to determine a vendor for the DNA extraction services.

IIB. Rapid Identification of Matched Donors – Objective 2: Primary DNA typing data can be used within the registry to improve the quality and resolution of volunteer donor HLA assignments.

IIB 2 Task 1:

Collection of Primary Data

Period 7 Activity:

- No activity this period.

IIB 2 Task 2: Validation of Logic of Primary Data – This task is closed.**IIB 2 Task 3:** Reinterpretation of Primary Data – This task is closed.**IIB 2 Task 4:**

Genotype Lists & Matching Algorithm

Period 7 Activity:

- No activity this period.

QUARTER PROGRESS REPORT

Development of Medical Technology for Contingency Response to Marrow Toxic Agents

July 01, 2013 through September 30, 2013

IIB. Rapid Identification of Matched Donors – Objective 3: Registry data on HLA allele and haplotype frequencies and on the nuances of HLA typing can be used to design computer algorithms to predict the best matched donor.

IIB.3 Task 1: Phase I of EM Haplotype Logic	Period 7 Activity: <ul style="list-style-type: none"> No activity this period.
IIB 3 Task 2: Enhancement of EM Algorithm	Period 7 Activity: <ul style="list-style-type: none"> The goal of this task is to validate allele predictions for various minority populations using NMDP registry donors. A total of 555 donors of Hispanic ethnicity were sent to a contract lab for 6 locus (A-B-C-DRB1-DQB1-DPB1) high resolution typing. These donors were previously identified as unspecified Hispanic. After participating in an ancestry questionnaire, where they were instructed to select a country of origin and give parental background information, their populations were specifically defined. High resolution typing results for these donors at all 6 loci of interest were received. Each donor's haplotype as predicted by the HapLogic III Haplostats tool will be compared to the actual typing of the donor as reported by the contract lab. The alleles will be predicted based off the original recruitment typing and the population the donor defined on the ancestry questionnaire. By comparing the Haplostats prediction to the actual typing, we will be able to detect potential inconsistencies or variation in the Hispanic sub-populations of the Caribbean islands and Mexico.
IIB 3 Task 3: Optimal Registry Size Analysis	Period 7 Activity: <ul style="list-style-type: none"> Drafted a MIBBI (Minimum Information for Biological and Biomedical Investigations) standard for Next Generation Sequencing (NGS) generation of HLA and KIR genotypes that identifies 10 key elements that must constitute an NGS HLA or KIR genotyping result. This NGS MIBBI standard will be presented at the third NGS Data Consortium meeting being held in Chicago in November in conjunction with the ASHI meeting. On behalf of the NGS Data Consortium, drafted a comment regarding the draft NIH Genomic Data Sharing Policy describing why highly polymorphic and poorly represented genomic regions such as the HLA and KIR regions require a higher data-sharing standard.

QUARTER PROGRESS REPORT**Development of Medical Technology for Contingency Response to Marrow Toxic Agents****July 01, 2013 through September 30, 2013**

	<ul style="list-style-type: none"> Staff integrated public resources at the IMGT/HLA Database to develop a table relating all HLA allele names and accession numbers across all available IMGT/HLA Database releases, for the purpose of assigning a likely IMGT/HLA Database release version to HLA datasets for which no such information is explicitly defined. Negotiated with the IMGT/HLA Database to make new versions of this table available as part of quarterly database releases going forward. This table will be integrated into the Toolkit for Immunogenomic Data Exchange and Storage (TIDES) for the purpose of identifying the appropriate GL Service instance under which to register a given GL String. Produced an HLA ambiguity resolution module that integrates reference allele frequencies, information about the geographic origin of a sample, and logic derived from our long experience in the field to identify the most likely pair of HLA alleles in any ambiguous HLA genotype. This module will be integrated into TIDES. Integrated the Push Immunogenomics to the Next Generation (PING) workflow into TIDES. PING functionality currently provides genotype calling for the killer immunoglobulin-like receptor (KIR) framework genes from NGS data, including whole exome and whole genome data.
IIB 3 Task 4: Target Under- Represented Phenotypes	Period 7 Activity: <ul style="list-style-type: none"> Preliminary data analysis for the ancestry questionnaire pilot (AQP) project was initiated. Thus far, data collection was completed for just over half (n=1021) of the projected sample. Work continued analyzing patterns of linkage disequilibrium for the HLA-DPA1 and HLA-DPB1 in non-Caucasian populations groups in the registry.
IIB 3 Task 5: Bioinformatics Web Site	Period 7 Activity: <ul style="list-style-type: none"> No activity this period.
IIB 3 Task 6: Improve Algorithm	Period 7 Activity: <ul style="list-style-type: none"> No activity this period.
IIB 3 Task 7: Population Genetics – This task is closed.	

QUARTER PROGRESS REPORT

Development of Medical Technology for Contingency Response to Marrow Toxic Agents

July 01, 2013 through September 30, 2013

IIB 3 Task 8: Haplotype Matching – This task is closed.

IIB 3 Task 9: Global Haplotype/Benchmark – This task is closed.

IIB. Rapid Identification of Matched Donors – Objective 4: Reducing the time and effort required to identify closely matched donors for patients in urgent need of HSC transplants will improve access to transplantation and patient survival in the context of a contingency response and routine patient care.

IIB.4 Task 1: Expand Network Communications – This task is closed.

IIB.4 Task 2:
Central Contingency
Management

Period 7 Activity:

African American (AFA) Few 10/10 Matched Donor Study

The AFA research study continued to evaluate NMDP process interventions for AFA searches, which included proactive HLA expert review of AFA patient searches, proactive donor contact to confirm interest and availability, and proactive donor HLA typing upgrades. This project will be instrumental in understanding the ability for process changes to increase AFA patients' chances to proceed to transplant, particularly in time of a contingency event. In the current quarter, 80 patients were selected for intervention, 942 donors had contact attempted on behalf of those patients, and 263 donors had HLA typing performed.

- CIBMTR provided support for the rapid identification of potential donors for newly diagnosed AML patients under the following clinical trial protocol:
 - S1203: A Randomized Phase III Study of Standard Cytarabine plus Daunorubicin (7+3) Therapy or Idarubicin with High Dose Cytarabine (IA) versus IA with Vorinostat (IA+V) in Younger Patients with Previously Untreated Acute Myeloid Leukemia (AML)
 - CIBMTR provided study-specific sample collection kits for patients, processed samples, arranged HLA typing, and generated preliminary search strategy reports to assist in the identification of donors and/or CBU through the NMDP.
 - It is anticipated that 750 patients will be accrued in less than 5 years with 40% needing HLA testing and search strategy results. The trial opened in April 2013. Activity during

QUARTER PROGRESS REPORT**Development of Medical Technology for Contingency Response to Marrow Toxic Agents****July 01, 2013 through September 30, 2013**

	<p>the quarter:</p> <ul style="list-style-type: none"> ▪ 51 patients enrolled and 54 sample collection kits distributed ▪ 10 patients identified as high risk <ul style="list-style-type: none"> • 12 HLA typings and preliminary search reports completed
IIB.4 Task 3: Benchmarking Analysis – This task is closed	
IIB.4 Task 4: Expand Capabilities of Collection and Apheresis Centers – This task is closed.	
IIC. Immunogenetic Studies – Objective 1: HLA mismatches may differ in their impact on transplant outcome, therefore, it is important to identify and quantify the influence of specific HLA mismatches. In contingency situations it will not be possible to delay transplant until a perfectly matched donor can be found.	
IIC.1 Task 1: Donor Recipient Pair Project	<p>Period 7 Activity:</p> <ul style="list-style-type: none"> • Activity on the Immunobiology Integration DataBase (IIDB) project: <ul style="list-style-type: none"> ○ Updated validation code to handle allele lists for a locus typing. ○ Updated validation code to correctly interpret common abbreviations and alternate formats ○ Updated match grade calculation to handle allele lists for a locus typing ○ The validation and match grade calculations now run daily. • Many HLA samples were prepared and typed for the ancestry projects, and the results from these data are presented in the quarterly report for Grant Award N00014-13-1-0039.
IIC. Immunogenetic Studies – Objective 2: Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.	
IIC 2 Task 1: Analysis of non-HLA loci	<p>Period 7 Activity:</p> <ul style="list-style-type: none"> • Immunobiology Integration Data Base (IIDB) <ul style="list-style-type: none"> ○ Implemented an HLA Validation Service that applies NMDP Operational rules for the

QUARTER PROGRESS REPORT**Development of Medical Technology for Contingency Response to Marrow Toxic Agents****July 01, 2013 through September 30, 2013**

	<p>validation of non-NMDP facilitated data (e.g. CIBMTR forms)</p> <ul style="list-style-type: none"> ○ Added non-NMDP-facilitated HLA typing information to the CIBMTR data warehouse and capability to compute HLA match grades using the NMDP HapLogic III algorithm. ● Clinical Ancestry Study <ul style="list-style-type: none"> ○ Pilot analysis has been complete, two analyses have been performed: <ul style="list-style-type: none"> ▪ Effect of donor/recipient genetic disparity on transplant outcome: Multivariate analysis on seven outcomes suggests there are trends worth investigating further. However, most p-values are not significant as the number of donor/recipient pairs in the discovery pilot is small ▪ Effect of recipient admixture on transplant outcome. Four main recipient admixtures were analyzed for all recipients in the pilot cohort: EUR, AFR, NAM and ASI. Again there are trends which require a larger sample to show statistical significance. ○ A power analysis was conducted for a second larger phase of the study that is currently being planned.
IIC 2 Task 2: Related Pairs Research Repository – This task is closed.	
IIC 2 Task 3: CIBMTR Integration – This task is closed.	
IID. Clinical Research in Transplantation – Objective 1: Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.	
IID.1 Task 1: Observational Research, Clinical Trials and NIH Transplant Center	<p>Period 7 Activity:</p> <p>Prospective Studies; RCI BMT</p> <ul style="list-style-type: none"> ● Staff worked with study team on final data cleaning and dataset preparation related to the 07-REV (Revlimid) trial. A final draft manuscript is currently being reviewed by the study team prior to submission for publication.
IID.1 Task 2: Research with NMDP Donors – This task is closed.	

QUARTER PROGRESS REPORT

Development of Medical Technology for Contingency Response to Marrow Toxic Agents

July 01, 2013 through September 30, 2013

IID.1 Task 3:

Expand Immunobiology Research

Period 7 Activity:

The CIBMTR IBWC met monthly during the quarter to discuss progress on ongoing research studies.

- Six abstracts were submitted and accepted:
 - Sarah Cooley, et al., *Recipient HLA-C1 enhances the clinical advantage of killer-cell immunoglobulin-like receptor B haplotype donors in myeloablative unrelated transplantation for acute Myelogenous leukemia*. ASH 2013 annual meeting, accepted for oral presentation.
 - John Koreth, et al., *HLA-mismatch is associated with worse outcomes after unrelated donor reduced intensity conditioning hematopoietic cell transplantation: A CIBMTR Analysis*. ASH 2013 annual meeting, accepted for oral presentation.
 - Salyka Sengsayadeth, et al., *Cytotoxic T lymphocyte antigen 4 (CTLA4) single nucleotide polymorphisms do not impact outcomes after unrelated donor transplant: A CIBMTR Analysis*. ASH 2013 annual meeting, accepted for oral presentation.
 - Michelle Gleason, et al., *A novel CD16xCD33 bispecific killer cell engager (BiKE) mediates a double hit for natural killer (NK) cells to target DC33+ myelodysplastic syndrome (MDS) cells and myeloid derived suppressor cells (MDSC) at all disease stages*. ASH 2013 annual meeting, accepted for oral presentation.
 - Ronald Sobecks, et al., *Influence of killer immunoglobulin-like receptor (KIR) and HLA genotypes on outcomes after reduced-intensity conditioning allogeneic hematopoietic stem cell transplantation for patients with AML and MDS: A report from the CIBMTR Immunobiology Working Committee*. ASH 2013 annual meeting, accepted for oral presentation.
 - Payal Khincha, et al., *Evaluating the utility of telomere length measurement by qPCR as a diagnostic test for dyskeratosis congenital*. ASH 2013 annual meeting, accepted for poster presentation.
- Three manuscripts were submitted:
 - Mary Eapen, et al., *Impact of allele-level HLA matching on outcomes after myeloablative*

QUARTER PROGRESS REPORT

Development of Medical Technology for Contingency Response to Marrow Toxic Agents

July 01, 2013 through September 30, 2013

	<p><i>single unit umbilical cord blood transplantation for hematologic malignancy</i>. Submitted to Blood.</p> <ul style="list-style-type: none">○ Katharina Fleischhauer, et al., <i>Risk-associations between HLA-DPB1 T cell epitope matching and outcome of unrelated hematopoietic cell transplantation are independent from HLA-DPA1</i>. Submitted to Blood○ Effie Petersdorf, et al., <i>HLA-C expression levels define permissible mismatches in hematopoietic cell transplantation</i>. Submitted to Nature Medicine. <ul style="list-style-type: none">• Four manuscripts were published:<ul style="list-style-type: none">○ Joseph Pidala, et al., <i>Amino acid substitution at peptide-binding pockets of HLA class I molecules increases risk of severe acute GVHD and mortality</i>. Blood, Aug. 27, 2013, Epub ahead of print○ Zaiba Shamim, et al., <i>Polymorphism in the interleukin-7 receptor-alpha and outcome after allogeneic hematopoietic cell transplantation with matched unrelated donor</i>. Scand J Immunol. 2013 Aug;78(2):214-20.○ Yasuo Morishima, et al., <i>Significance of ethnicity in the risk of acute graft-versus-host disease and leukemia relapse after unrelated donor hematopoietic stem cell transplantation</i>. Biol Blood Marrow Transplant. 2013 Aug;19(8):1197-203.○ Noriko Isobe, et al., <i>Genetic risk variants in African Americans with multiple sclerosis</i>. Neurology. 2013 Jul 16;81(3):219-27.
--	---

QUARTER PROGRESS REPORT**Development of Medical Technology for Contingency Response to Marrow Toxic Agents****July 01, 2013 through September 30, 2013****ACRONYM LIST**

AABB	American Association of Blood Banks	HML	Histoimmunogenetics Mark-up Language
AFA	African American	HR	High Resolution
AFR	African American	HRSA	Health Resources and Services Administration
AGNIS	A Growable Network Information System	HSC	Hematopoietic Stem Cell
ABD	Antigen Binding Domain	IBWC	Immunobiology Working Committee
AML	Acute Myelogenous Leukemia	ICRHER	International Consortium for Research on Health Effects of Radiation
API	Asian Pacific Islander	IIDB	Immunobiology Integration Data Base
AQP	Ancestry Questionnaire Project	IDM	Infectious Disease Markers
ARS	Acute Radiation Syndrome (also known as Acute Radiation Sickness)	IHWG	International Histocompatibility Working Group
ASBMT	American Society for Blood and Marrow Transplantation	IMGT	International ImMunoGeneTics
ASHI	American Society for Histocompatibility and Immunogenetics	IPR	Immunobiology Project Results
ASI	Asian	IND	Investigational New Drug
ASTHO	Association of State and Territorial Health Officials	IS	Information Services
B-LCLs	B-Lymphoblastoid Cell Lines	IT	Information Technology
BARDA	Biomedical Advanced Research and Development Authority	IRB	Institutional Review Board
BBMT	Biology of Blood and Marrow Transplant	JCAHO	Joint Commission on Accreditation of Healthcare Organizations
BCP	Business Continuity Plan	KIR	Killer Immunoglobulin-like Receptor
BCPeX	Business Continuity Plan Exercise	MDACC	MD Anderson Cancer Center
BMCC	Bone Marrow Coordinating Center	MDS	Myelodysplastic Syndrome
BMDW	Bone Marrow Donors Worldwide	MHC	Major Histocompatibility Complex
BMT	Bone Marrow Transplantation	MICA	MHC Class I-Like Molecule, Chain A
BMT CTN	Blood and Marrow Transplant - Clinical Trials Network	MICB	MHC Class I-Like Molecule, Chain B

QUARTER PROGRESS REPORT

Development of Medical Technology for Contingency Response to Marrow Toxic Agents

July 01, 2013 through September 30, 2013

BODI	Business Objects Data Integrator	MKE	Milwaukee
BRT	Basic Radiation Training	MRD	Minimal Residual Disease
C&A	Certification and Accreditation	MSKCC	Memorial Sloan-Kettering Cancer Center
CAU	Caucasian	MSP	Minneapolis
		MUD	Matched Unrelated Donor
CBMTG	Canadian Blood and Marrow Transplant Group	MULTI	Multiple
CBB	Cord Blood Bank	NAC	Nuclear Accident Committee
CBC	Congressional Black Caucus	NACCHO	National Association of County & City Health Officials
CBS	Canadian Blood Service	NAM	Native American
CBU	Cord Blood Unit	NARR	National Alliance for Radiation Readiness
CD	Cell Differentiation	NCBI	National Center for Biotechnology Information
CDA	Clinical Document Architecture	NCBM	National Conference of Black Mayors
CFU	Colony Forming Unit	NCI	National Cancer Institute
CHORI	Children's Hospital of Oakland Research Institute	NDMS	National Disaster Medical System
CHTC	Certified Hematopoietic Transplant Coordinator	NEMO	N-locus Expectation-Maximization using Oligonucleotide typing data
CIBMTR®	Center for International Blood & Marrow Transplant Research	NGS	Next Generation Sequencing
CIT	CIBMTR Information Technology	NHLBI	National Heart Lung and Blood Institute
CLIA	Clinical Laboratory Improvement Amendment	NIH	National Institutes of Health
CMCR	Centers for Medical Countermeasures Against Radiation	NIMA	Non-Inherited Maternal Antigen
CME	Continuing Medical Education	NIMS	National Incident Management System
CMF	Community Matching Funds	NK	Natural Killer
CMV	Cytomegalovirus	NLE	National Level Exercise
CNV	Copy Number Variation	NMDP®	National Marrow Donor Program
COG	Children's Oncology Group	NRP	National Response Plan
CREG	Cross Reactive Groups	NST	Non-myeloablative Allogeneic Stem Cell Transplantation

QUARTER PROGRESS REPORT**Development of Medical Technology for Contingency Response to Marrow Toxic Agents****July 01, 2013 through September 30, 2013**

CSS	Center Support Services	OCR/ICR	Optical Character Recognition/Intelligent Character Recognition
CT	Confirmatory Testing	OIT	Office of Information Technology
CTA	Clinical Trial Application	OMB	Office of Management and Budget
CTMS	Clinical Trial Management System		
DC	Donor Center	ONR	Office of Naval Research
DCB	Double Cord Blood		
DHHS-ASPR	Department of Health and Human Service – Assistant Secretary Preparedness and Response	P2P	Peer-to-Peer
DIY	Do it yourself	PBMC	Peripheral Blood Mononuclear Cells
DKMS	Deutsche Knochenmarkspenderdatei	PBSC	Peripheral Blood Stem Cell
DMSO	Dimethylsulphoxide	PCR	Polymerase Chain Reaction
DoD	Department of Defense	PSA	Public Service Announcement
DNA	Deoxyribonucleic Acid	QC	Quality control
DR	Disaster Recovery	RCC	Renal Cell Carcinoma
D/R	Donor/Recipient	RCI BMT	Resource for Clinical Investigations in Blood and Marrow Transplantation
DSTU	Draft Standard for Trial Use	REAC/TS	Radiation Emergency Assistance Center/Training Site
EBMT	European Group for Blood and Marrow Transplantation	REST	Representational State Transfer
ED	Emergency Department	RFP	Request for Proposal
EDC	Electronic Data Capture	RFQ	Request for Quotation
EFI	European Federation of Immunogenetics	RG	Recruitment Group
EM	Expectation Maximization	RITN	Radiation Injury Treatment Network
EMDIS	European Marrow Donor Information System	SBT	Sequence Based Typing
ENS	Emergency Notification System	SCTOD	Stem Cell Therapeutics Outcome Database
ERSI	Environment Remote Sensing Institute	SG	Sample Group
EUR	European	SHF	Synthetic Haplotype Frequency
FBI	Federal Bureau of Investigation	SLCBB	St. Louis Cord Blood Bank
FDA	Food and Drug Administration	SLW	STAR Link® Web
FDR	Fund Drive Request	SSA	Search Strategy Advice

QUARTER PROGRESS REPORT**Development of Medical Technology for Contingency Response to Marrow Toxic Agents****July 01, 2013 through September 30, 2013**

FLOCK	Flow Cytometry Analysis Component	SSO	Sequence Specific Oligonucleotides
Fst	Fixation Index	SSP	Sequence Specific Primers
GETS	Government Emergency Telecommunications Service	SSOP	Sequence Specific Oligonucleotide Probes
GCSF	Granulocyte-Colony Stimulating Factor (also known as filgrastim)	STAR®	Search, Tracking and Registry
GIS	Geographic Information System	TC	Transplant Center
GS	General Services	TED	Transplant Essential Data
GTR	Genetic Testing Registry	TNC	Total Nucleated Cell
GvHD	Graft vs Host Disease	TSA	Transportation Security Agency
HCS®	HealthCare Standard	UCSF	University of California – San Francisco
HCT	Hematopoietic Cell Transplantation	UI	User Interface
HEPP	Hospital Emergency Preparedness Program	UML	Unified Modeling Language
HHQ	Health History Questionnaire	URD	Unrelated Donor
HHS	Health and Human Services	WGA	Whole Genome Amplification
HIPAA	Health Insurance Portability and Accountability Act	WMDA	World Marrow Donor Association
HIS	Hispanic	WU	Work-up
HLA	Human Leukocyte Antigen		